

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions and listings of claims in the application. Please amend the claims as follows:

Claims 1-20. (Canceled)

21. (Withdrawn) A method of producing a transgenic mouse comprising a vector, comprising:

a) introducing a vector into murine embryonic stem (ES) cells, wherein the vector comprises:

i) a 5' gene trap cassette, comprising in operable combination:

1) a splice acceptor;

2) a first exon sequence located 3' to said splice acceptor, said first exon sequence encoding a marker enabling the identification of a cell expressing said first exon sequence; and

3) a polyadenylation sequence located at the 3' end of said first exon sequence;

ii) a 3' gene trap cassette located 3' to said polyadenylation sequence, comprising in operable combination:

1) a first promoter;

2) a second exon sequence located 3' from and expressed by said first promoter, said second exon sequence not encoding an activity conferring antibiotic resistance;

3) a splice donor sequence located at the 3' end of said second exon sequence; and

wherein said vector does not encode a promoter mediating the expression of said first exon sequence, and wherein said vector does not encode a sequence that mediates the polyadenylation of an mRNA transcript encoded by said second exon sequence;

b) selecting a murine ES cell that comprises the vector; and

c) making a transgenic mouse comprising the vector from the selected murine ES cell that comprises the vector.

22. (Withdrawn) The method of claim 21, wherein the vector from the selected murine ES cell that comprises the vector is non-homologously incorporated into the genome of at least one cell in the transgenic mouse.

23. (Withdrawn) The method of claim 22, further comprising identifying at least one trapped cellular exon after (b).

24. (Withdrawn) The method of claim 22, further comprising identifying at least one trapped cellular exon after (c).

25. (Withdrawn) The method of claim 21, wherein the transgenic mouse comprising the vector is a somatic transgenic mouse.

26. (Withdrawn) The method of claim 21, wherein the transgenic mouse comprising the vector is a germ line transgenic mouse.

27. (Withdrawn) The method of claim 21, wherein the first exon sequence additionally encodes an internal ribosome entry site operatively positioned between said splice acceptor and an initiation codon of said first exon.

28. (Withdrawn) The method of claim 21, wherein the vector additionally comprises in the region between said polyadenylation sequence and said first promoter at least one

of a transcription termination sequence, a 3' terminal exon, and a sequence encoding a self-cleaving RNA.

29. (Withdrawn) The method of claim 21, wherein the marker encoded by the first exon sequence of the vector is selected from a marker conferring antibiotic resistance, a marker conferring antibiotic sensitivity, an enzymatic marker, a recombinase, and a fluorescent marker.

30. (Withdrawn) The method of claim 29 wherein the marker confers neomycin resistance.

31. (Withdrawn) The method of claim 21, wherein the vector is selected from a viral vector and a retroviral vector.

32. (Withdrawn) The method of claim 23, wherein the identifying at least one trapped cellular exon comprises:

- a) obtaining a chimeric transcript resulting from splicing of the second exon sequence to a third exon sequence, wherein the third exon sequence is from the genome of the ES cell;
- b) reverse transcribing said chimeric transcript to produce a cDNA template; and
- c) determining the polynucleotide sequence of the cDNA template.

33. (Withdrawn) The method of claim 24, wherein the identifying at least one trapped cellular exon comprises:

- a) obtaining a chimeric transcript resulting from splicing of the second exon sequence to a third exon sequence, wherein the third exon sequence is from the genome of the transgenic mouse;
- b) reverse transcribing said chimeric transcript to produce a cDNA template; and

c) determining the polynucleotide sequence of the cDNA template.

34. (Currently amended) A method of making a transgenic mouse comprising a vector, comprising:

a) introducing a vector into a collection of murine mouse embryonic stem (ES) cells, wherein the vector comprises a 3' gene trap cassette, comprising in operable combination:

i) a promoter;

ii) an exon sequence located 3' from and expressed by said first promoter, said exon sequence not encoding an activity conferring antibiotic resistance; and

iii) a splice donor sequence located at the 3' end of said exon sequence;

wherein the vector does not encode a sequence that mediates the polyadenylation of an mRNA transcript encoded by said exon sequence;

b) selecting ~~a murine ES cell~~ mouse ES cells that comprise[[s]] the vector integrated into the genome; and

c) identifying at least one mouse ES cell comprising the vector, wherein the integration of said vector results in the mutation of a gene of the mouse, and wherein the mutated gene has been identified after integration of the vector; and

[[c)] d) making a transgenic mouse comprising the vector from at least one identified ~~the selected murine mouse~~ ES cell that comprises the vector.

35. (Currently amended) The method of claim 34, wherein the vector from ~~the selected murine~~ at least one identified mouse ES cell that comprises the vector is non-homologously incorporated into the genome of at least one cell in the transgenic mouse.

36. (Canceled) ~~The method of claim 35, further comprising identifying at least one trapped cellular exon after (b).~~
37. (Canceled) ~~The method of claim 35, further comprising identifying at least one trapped cellular exon after (c).~~
38. (Previously presented) The method of claim 34, wherein the transgenic mouse comprising the vector is a somatic transgenic mouse.
39. (Previously presented) The method of claim 34, wherein the transgenic mouse comprising the vector is a germ line transgenic mouse.
40. (Currently amended) The method of claim 34, wherein the exon sequence additionally encodes an internal ribosome entry site operatively positioned between said ~~splice acceptor~~ promoter and an initiation codon of said exon sequence.
41. (Currently amended) The method of claim 34, wherein the vector additionally comprises in the region upstream of ~~between said polyadenylation sequence and~~ said promoter at least one of a transcription termination sequence, a 3' terminal exon, and a sequence encoding a self-cleaving RNA.
42. (Previously presented) The method of claim 34, wherein the exon sequence encodes a marker selected from an enzymatic marker, a recombinase, and a fluorescent marker.
43. (Previously presented) The method of claim 42 wherein the marker is a fluorescent marker.
44. (Previously presented) The method of claim 34, wherein the vector is selected from a viral vector and a retroviral vector.

45. (Currently amended) The method of claim ~~[[36]]~~ 34, wherein the mutated gene has been identified by a method comprising: identifying at least one trapped cellular exon-

comprises:

- a) obtaining a chimeric transcript resulting from splicing of the exon sequence from the vector to a second exon sequence, wherein the second exon sequence is from the genome of the ES cell;
- b) reverse transcribing said chimeric transcript to produce a cDNA template; and
- c) determining the polynucleotide sequence of the cDNA template.

46. (Canceled) ~~The method of claim 37, wherein the identifying at least one trapped cellular exon comprises:~~

- ~~a) obtaining a chimeric transcript resulting from splicing of the exon sequence from the vector to a second exon sequence, wherein the second exon sequence is from the genome of the transgenic mouse;~~
- ~~b) reverse transcribing said chimeric transcript to produce a cDNA template; and~~
- ~~c) determining the polynucleotide sequence of the cDNA template.~~